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Date: January 2, 2009

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
Before the Board of Patent Appeals and Interferences

Appellants:	Nicholas L. Abbott, et al.	Group Art Unit:	1641
Serial No.:	10/711,517	Examiner:	Foster, Christine E.
Filed:	September 23, 2004	Attorney Docket. No.:	960296.00526

Title: USING LIQUID CRYSTALS TO DETECT AFFINITY MICROCONTACT PRINTED BIOMOLECULES

APPELLANTS' BRIEF ON APPEAL

Mail Stop Appeal Brief
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Appellants, Nicholas L. Abbott, Matthew L. Tingey, Brian H. Clare and Chang-Hyun Jang, having filed a timely Notice of Appeal in the above-identified patent application, hereby submit this brief.

I. REAL PARTY IN INTEREST

The real party in interest is the Wisconsin Alumni Research Foundation, Madison, Wisconsin, which is the assignee of this patent application.

II. RELATED APPEALS, JUDICIAL PROCEEDINGS AND INTERFERENCES

There are no related appeals, judicial proceedings or interferences.

III. STATUS OF CLAIMS

Claims 7-9 and 12-13 were previously canceled by Appellants. Claims 1-6, 10, 11, and 14-41 are currently pending. Claims 24-41 were previously withdrawn from consideration. Claims 1-6, 10, 11, and 14-23 stand finally rejected. This appeal is taken with respect to the finally rejected pending claims 1-6, 10, 11, and 14-23, which are set forth in the attached Claims Appendix A.

IV. STATUS OF AMENDMENTS

All amendments submitted by Appellants have been entered. No new amendments were submitted after final rejection.

V. SUMMARY OF THE CLAIMED SUBJECT MATTER

The appealed claims include one independent claim: claim 1. In addition, the appealed claims include seventeen claims depending from independent claim 1: claims 2-6, 10, 11 and 14-23.

Claim 1 is directed at a method for detecting a ligand in a sample. The first step of claim1 requires contacting a sample having a ligand with an affinity substrate. The affinity substrate contains a receptor capable of specifically binding the ligand, and the receptor binds the ligand upon contact with the sample. In the second step recited in claim 1, the affinity substrate containing the bound ligand is contacted with a detection surface. In this step, the ligand is transferred to the detection surface. In the third step recited in claim 1, the presence of the ligand on the detection surface is detected by contacting the detection surface with a liquid crystal. A change in the orientation of the liquid crystal in contact with the detection surface indicates the presence of the ligand.

The method is explained in detail in paragraph [0055] of Appellants' as-filed specification. Note that as explained in paragraph [0055], the first step is sometimes referred to as "inking" the stamp (the affinity substrate), and the second step is sometimes referred to as "stamping" or "printing" the ligand onto the detection surface. As further described in paragraph [0056], the process is generally illustrated in Figure 1.1, and a specific example of the process is illustrated in Figure 1.2. A detailed discussion of the affinity substrate begins at paragraph [0065], and a detailed discussion of the detection surface begins at paragraph [0084]. Paragraphs [0100] –

[0103] discuss the use of liquid crystal to detect the presence of the ligand on the detection surface. Detailed examples using the method are presented beginning in paragraph [0109].

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Claims 1-6, 10-11, 15-20 and 22-23 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Appellants regard as the invention.

Claims 1-6, 10-11, 15-20 and 22-23 stand rejected under 35 U.S.C. §103(a) as being unpatentable over either Bernard et al. (Nature Biotechnology 19:866-869 (2001)) or Renault et al. (Agnew. Chem. Int. Ed. 41: 2320-2323 (2002)) in view of Abbott et al. (U.S. Pat. No. 6,284,197).

Claim 14 stands rejected under 35 U.S.C. §103(a) as being unpatentable over either Bernard et al. (Nature Biotechnology 19:866-869 (2001)) or Renault et al. (Agnew. Chem. Int. Ed. 41: 2320-2323 (2002)) in view of Abbott et al. (U.S. Pat. No. 6,284,197) as applied to claim 1, and further in view of Tang et al. (U.S. Patent No. 5,886,195).

Claim 21 stands rejected under 35 U.S.C. §103(a) as being unpatentable over either Bernard et al. (Nature Biotechnology 19:866-869 (2001)) or Renault et al. (Agnew. Chem. Int. Ed. 41: 2320-2323 (2002)) in view of Abbott et al. (U.S. Pat. No. 6,284,197) as applied to claim 1, and further in view of Choi et al. (U.S. Patent No. 6,293,296).

VII. ARGUMENT

A. REJECTIONS UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

1. Summary of the rejections.

The Office has taken issue with the language in claim 1, step (c), "detecting the presence of the ligand on the detection surface by contacting the detection surface with liquid crystal, wherein the presence of the ligand on the detection surface is detected *by a change in the orientation of the liquid crystal* contacted with the detection surface" (Examiner's emphasis). The Office apparently believes it is not clear what the change in orientation of the liquid crystal would be assessed relative to, since the Office believes the liquid crystal would not yet be oriented or anchored on the surface before ligand binding. Therefore, the Office finds it unclear as to how a "change in orientation" would be assessed. The Office poses the question "is the change relative to the orientation of liquid crystals on a controlled detection surface having no printed ligand? Or

relative to other areas of the surface not contacted by the affinity substrate?" (Final Office Action, page 3.)

2. Because the meaning of the rejected claims is clear when properly viewed in light of the specification, the rejections are clear error of law.

Because the Office failed to examine the claims as required under the proper legal framework, this rejection is improper. In reviewing a claim for compliance with 35 U.S.C. §112, second paragraph, the Examiner must consider the claims as a whole to determine whether the claim apprises the skilled artisan of its scope, and therefore serves the required notice function by providing clear warning to others as to what constitutes infringement of the claim. MPEP 2173.02, citing *Solomon v. Kimberly-Clark Corp.*, 216 F.3d 1372, 1379 (Fed. Cir. 2000). Definiteness of claim language is to be analyzed, not in a vacuum, but in light of the content of the disclosure and the teachings of the prior art. MPEP 2173.02. The proper test is whether "those skilled in the art would understand what is claimed when the claim is read in light of the specification." *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565, 1576 (Fed. Cir 1986). If one skilled in the art is able to ascertain the meaning of the claim in light of the specification, 35 U.S.C. §112, second paragraph, is satisfied. *Id.*

Appellants respectfully submit that the Office erred in not considering the meaning of the rejected claims in light of the specification. In light of the specification, "change in orientation" clearly means that the orientation of the liquid crystal in contact with the detection surface varies between areas of the detection surface containing bound ligand and areas of the detection surface that do not contain bound ligand.

Paragraph [0055] of the specification explains that a disordering or disruption of the liquid crystal on a detector surface (i.e. inconsistent orientation of the liquid crystal in contact with the detection surface) indicates the presence of the ligand on the detector surface. This is further clarified in Figure 1.1, which illustrates in general how the claimed method works. On the bottom of the figure is a drawing showing the change in orientation of the liquid crystal. The drawing shows that the recited change in orientation is clearly a change in the orientation of the liquid crystal in contact with regions of the detection surface containing the bound ligand relative to the orientation of liquid crystal in contact with regions of with the same detection surface that do not contain the bound ligand.

Further, Figure 13 (explained in paragraph [0208]) shows liquid crystal alignment in both a stamped (WT) and control (parental) situation. As shown in the twelve hour results and explained

further in paragraph [0208], the printed samples showed disruption *in the printed regions* (as compared to the non-printed regions, emphasis added), while the control samples did not. It is this difference in orientation between the liquids crystal in contact with the printed regions of a detection surface as compared to the orientation of the liquid crystal in contact with the non-printed regions of the same surface that allows for the optical detection of the ligands in the printed regions by visual contrasts in the optical image. See optical image at upper right in Fig. 13. No such contrast and detection is present in the control surface. See optical image at lower right in Fig. 13.

Thus, when viewed in light of the specification, it is clear that the recited change in the orientation of the liquid crystal are the changes that occur at the regions of the detection surface containing bound ligand relative to the liquid crystal orientation at other regions of the detection surface where ligand is not present. Because the meaning of the rejected claims is clear when properly considered in light of the specification, Appellants respectfully ask the Board to reconsider and reverse these rejections.

B. REJECTIONS UNDER 35 U.S.C. § 103(A) OVER BERNARD OR RENAULT IN VIEW OF ABBOTT

1. Summary of the rejections.

The Office has rejected claims 1-6, 8-11, 13, 15-20 and 22-23 as obvious over Bernard et al. or, alternatively, Renault et al. in view of Abbott et al. Specifically, the Office alleges that Bernard et al. teach a method of detecting a ligand comprising the step of (a) contacting a sample having a ligand (e.g., ^{125}I-IgG) with an affinity substrate (PDMS stamp) wherein the affinity substrate comprises an array of receptors that are capable of specifically binding the ligand. The Office further alleges that Bernard et al. teach a step (b) of contacting the affinity substrate with a detection surface (glass or polystyrene) wherein a portion of the ligand that is bound by the receptor is transferred to the detection surface. Bernard et al. apparently fail to teach detection of the ligand on the detection surface by liquid crystal but, instead, utilize radioactive or fluorescent labels attached to the target ligands (Final Action, pages 4-5).

In similar fashion, the Office alleges that Renault et al. teach a method of detecting a ligand (e.g., an antibody) by contacting a ligand-containing sample with an affinity substrate (PDMS stamp), followed by transfer of the ligand to a detection surface where detection of the ligand is accomplished by fluorescent or gold-labeled antibodies via fluorescence microscopy or

atomic force microscopy. Renault et al. fail to teach detection of the ligand via liquid crystal techniques (Final Action pages 5-6).

The Office alleges that Abbott et al. teach a device having a detection surface to which a ligand may be transferred and its presence subsequently detected by using a liquid crystal. The Office states one of skill would have been motivated to combine the teachings of Bernard et al. and Abbott et al. or, alternatively, Renault et al. and Abbott et al., because Abbott et al. teach that liquid crystal detection surfaces do not require prelabeling of the ligand and, as such, one would be motivated to stamp the affinity-captured ligand onto the device of Abbott et al. in order to avoid the need for fluorescent or labels of the ligands. The Office further states that "one would have a reasonable expectation of success in affinity stamping the surface of Abbott et al. according to the methods of Bernard et al. or Renault et al. because the surface of Abbott et al. is compatible with microcontact printing." The Office refers Appellants to the reference by Abbott et al. at column 17, lines 5-22 to support this conclusion (Final Action pages 6-8).

Claim 1 recites a method for detecting a ligand in a sample comprising: (a) contacting a sample having a ligand with an affinity substrate, wherein the affinity substrate comprises a receptor capable of specifically binding said ligand, the receptor binding the ligand upon contact with the sample; (b) contacting the affinity substrate with a detection surface, wherein the ligand which is bound to the receptor is transferred to the detection surface; and (c) detecting the presence of the ligand on the detection surface by contacting the detection surface with a liquid crystal, wherein the presence of the ligand on the detection surface is detected by a change in the orientation of the liquid crystal contacted with the detection surface. Because (1) the Examiner erred in not properly considering and applying in a patentability analysis Appellants' rebuttal evidence (the Abbott §1.132 Declaration attached to the Evidence Appendix B); (2) the skilled artisan at the time of the invention would not have had a reasonable expectation of success in combining the cited documents to practice the steps recited in claim 1; (3) the skilled artisan at the time of the invention would not have had a motivation to combine the cited documents to practice the steps recited in claim 1; and (4) the rejection is improperly based on hindsight reconstruction, Appellants respectfully request that the Board reconsider and reverse the rejections.

2. Because the Office clearly erred by not properly considering Appellants' rebuttal evidence presented in the Abbott §1.132 Declaration, the rejections are improper and should be reversed.

When a patent applicant submits evidence supporting the patentability of one or more claims and rebutting the Office's contention that the claims are obvious, the Office must reconsider the patentability of the invention. MPEP 716.01(d). Specifically, the Office is required to carefully consider the newly submitted evidence. *In re Sullivan*, 498 F. 3d 1345, 1351, 81 USPQ2d 1034 (Fed. Cir. 2007); *In re Soni*, 54 F.3d 746, 750 (Fed.Cir.1995); *In re Sernaker*, 702 F.2d 989, 996 (Fed.Cir.1983). If, after evaluating the newly submitted evidence, the Office is still not convinced that the claimed invention is not patentable, the next Office action must include a statement to that effect and identify the reasons why the Office remains unconvinced. MPEP 716.01(d) (citing *Demaco Corp. v. F. Von Langsdorff Licensing Ltd.*, 851 F.2d 1387 (Fed. Cir.), *cert. denied*, 488 U.S. 956 (1988)). The reasons identified must be specific; general statements without an explanation supporting such findings are not sufficient. MPEP 716.01.

A finding of obviousness under 35 U.S.C. § 103 is a legal conclusion based on underlying findings of fact. *Sullivan* at 1350 (citing *In re Kotzab*, 217 F.3d 1365, 1369 (Fed.Cir.2000)). With respect to the instant invention, the Office has failed to establish a *prima facie* case of obviousness because (1) the facts and conclusions about the cited documents that the Office has relied on are scientifically inaccurate and, (2) the Office has failed to properly consider the facts submitted in rebuttal to correct such inaccuracies. In particular, the Office has made scientifically incorrect assumptions about the teachings of Abbott.

In the Office Action of April 10, 2007, the Office asserted that "[o]ne would have reasonable expectation of success in affinity stamping the surface of Abbott et al. according to the method of Bernard et al. or Renault et al. because the surface of Abbott et al. is compatible with microcontact printing." The assumption contained in this assertion is that affinity microcontact printing is similar to and easily substituted for the types and functions of microcontact printing described in Abbott et al. This assumption is illustrated again on page 28 of the Action, where the Office responded to Appellants' previous arguments by asserting that "even if Abbott et al. teach microcontact printing in another sense, such a teaching is nonetheless relevant to the instant rejection since it establishes that the detection surface of Abbott et al. is compatible with microcontact printing, such that one would have a reasonable expectation of success in applying

the ligand to the detection surface of Abbott et al. by the microcontact printing method of Bernard et al." (i.e. affinity microcontact printing).

To provide evidence that affinity microcontact printing is substantially different than the microcontact printing methods disclosed by Abbott et al., Appellants submitted with the response of October 10, 2007 the §1.132 Declaration of Dr. Nicholas Abbott, a coinventor in both Abbott et al. and the present application. The Declaration is attached to this Appellate Brief at Evidence Appendix B. The Declaration was submitted to correct the Office's scientifically inaccurate assumption that affinity microcontact printing is similar to and easily substituted for the microcontact printing methods disclosed in Abbott et al. This inaccurate assumption was used by the Office in arguing that the elements of the cited documents could be combined into the present invention with a reasonable expectation of success. In the Declaration, Dr. Abbott explains the important distinctions between affinity microcontact printing and the microcontact printing method mentioned in Abbott et al. Microcontact printing as mentioned in Abbott et al. is one of various methods that could be used in the microfabrication of structured surfaces, or substrates, on which molecular interactions can be detected using liquid crystal. See Declaration paragraph 6. While Abbott et al. suggest the use of microcontact printing to prepare structured substrate surfaces, such as gold and silicon micro and nanostructures, this is quite different than the delivery of analytes to a previously prepared structured substrate surface, or affinity microcontact printing. *Id.*

Indeed, as Dr. Abbott explains, affinity microcontact printing is not mentioned in any context by Abbott et al, nor is it disclosed in the present application as a tool for microfabrication of device surfaces. *Id.* Instead, it is disclosed in the present invention only as an analyte transfer tool. *Id.* Thus, affinity microcontact printing is a different tool with different uses than the surface microfabrication tools mentioned in Abbott et al. (including microcontact printing). A review of the Declaration clearly shows that the two different microcontact printing tools are not readily substitutable, and the Office's assumption supporting a reasonable expectation of success in combining the elements of the cited documents to make the presently claimed invention is clear error. Thus, the rejections based on that assumption should be reversed.

The Office committed further error when, instead of carefully considering the rebuttal evidence of October 10, 2007, as required by law, the Office ignored the distinctions set forth in the Abbott §1.132 Declaration and summarily dismissed the Declaration as containing evidence

"tangential to the instant rejection" and as representing "an attempt to rebut a position that has not been taken by the Office." Final Office Action page 17. Thus without addressing the substance of the Declaration, the Office simply reiterated its previous argument that the detection substrates of Abbott et al. are compatible with microcontact printing, and that this compatibility is evidence that there would be a reasonable expectation of success in combining the elements of the cited documents to make the present invention. Final Office Action pages 8, 16-17.

Ignoring the requirement that timely submitted evidence of obviousness must be carefully considered and that specific reasons why the evidence is unpersuasive must be provided, the Office simply does not address the Dr. Abbott's explanation of affinity microcontact printing as a completely different tool used for a different purpose than the microcontact printing mentioned in Abbott et al. Instead, the Action ignored the distinction explained in the Declaration and reiterated the inaccurate assumption that they are the same process used in different contexts. Although Dr. Abbott rebutted this assumption, the Office has dismissed the rebuttal as "tangential."

This summary dismissal of Appellants' evidence is clear error of both fact and law. It is error of fact, because the Office continued to make the same scientifically inaccurate assumption regarding affinity microcontact printing and the microcontact printing technique mentioned in Abbott et al. after the Declaration evidence was presented, and used that assumption in justifying the rejections. It is error of law, because the Office is required to consider the additional evidence and to give specific reasons as to why the evidence is not persuasive regarding patentability. The Office appears to have done neither.

Because the Office committed clear error of fact and law in these claims rejections, Appellants respectfully request that the Board reconsider and reverse these rejections.

3. Because the skilled artisan would not have had a reasonable expectation of success in combining the teachings of the cited documents into the method recited in the rejected claims, the rejections are improper.

To reject a claim based on a motivation to combine prior art reference teachings to arrive at a claimed invention, the Office must articulate a finding that the artisan would have had a reasonable expectation of success in combining the reference teachings. MPEP 2143(G). Here, in view of the lack of teachings/guidance provided in the cited references or any general knowledge

available to the artisan at the time of the invention and, there would have been no reasonable expectation of success and predictability of results in combining the prior known elements.

The successful detection of affinity stamped ligand on a detection surface by liquid crystal, as opposed to ligand detection by fluorescent or radioactive labeling, is far from a mere substitution of one known element for another to obtain predictable results. The two detection methods work on completely different principles and have completely different uses. Keeping Appellant's claimed subject matter in mind, it is apparent that Bernard et al. do not teach nor do they suggest the use of a detection surface upon which a ligand may be stamped and liquid crystal detection subsequently carried out.

Bernard et al. are limited in their teaching to the use of a polystyrene substrate for affinity stamping. As well, Renault et al. fail to teach or suggest the presently claimed elements and only teach glass as a stamping substrate. No further teaching as to selection of suitable detection surfaces is provided, and certainly no expectation of success for combining affinity microcontact printing with liquid crystal detection is indicated. Combining affinity microcontact printing with liquid crystal detection is simply not contemplated by these two cited references; no teaching is provided by Bernard et al. and Renault et al. to guide an artisan in the context of liquid crystal detection.

While the cited reference to Abbott et al. describes a wide variety of surfaces suitable for liquid crystal detection, including a general mention of self assembled monolayers, the method of detecting affinity microcontact printed ligands via detection surfaces compatible with liquid crystals is not disclosed or suggested by Abbott et al. At most, Abbott et al. recognizes various materials that may be used in the practice of liquid crystal detection and does not show or suggest that detection surfaces may also act to receive a ligand to be detected from an affinity substrate.

In arriving at its conclusion that the detection surface of Abbott et al. is compatible with affinity microcontact printing, the Office cites to column 17, lines 5-22 of the reference to Abbott et al. where mention to microcontact printing is made in the context of patterning a detection surface (termed a "detection substrate"). Final Action page 8. It should be noted that "affinity" microcontact printing is not mentioned in the Abbott et al. reference. In fact, the transfer of a ligand to be detected by any microcontact printing technique is not described by Abbott et al. Instead, Abbott et al. discuss microcontact printing in the context of forming patterns ("as small as 200 nm") such as, "wells, enclosures, partitions, recesses, inlets, outlets, channels, troughs,

diffraction gratings and the like." The discussion of microcontact printing by Abbott et al. is, in fact, in an unrelated context to the transfer of ligand by "affinity" microcontact printing taught by Bernard et al. and Renault et al. Therefore, the Office's contention that the detection surfaces taught by Abbott et al. are generally compatible with affinity microcontact printing in that the artisan would expect success in ligand detection via liquid crystal methodology is unfounded.

In order to aid the Board in its appreciation of this central issue, the Board is again directed to the statement of Dr. Nicholas Abbott, a co-inventor in this case and in Abbott et al. The statement is contained in the Rule 1.132 Declaration attached to the evidence appendix (Appendix B) of this Brief. The Declaration was entered into the record with Appellants' response of October 10, 2007.

The Board is referred to paragraphs 5 and 6 of the Declaration, where Dr. Abbott addresses the discussion of microcontact printing in U.S. Patent 6,284,197. Dr. Abbott clearly indicates that the previous teaching regarding microcontact printing was in the context of fabricating detection surfaces, a pre-detection activity. In contrast, the presently claimed invention is directed to using a specific type of microcontact printing, namely affinity microcontact printing to carry out delivery of a ligand to be analyzed by a detection surface. The substitution of the detection methods described in his previous patent (i.e., the Abbott et al. reference) for fluorescent or radioactive labeling described by Renault et al. and Bernard et al. would not have been prompted by design incentives as the artisan, after considering the cited documents and general knowledge, would not have predicted a successful result due to the lack of available guidance in the art for combining affinity microcontact printing with liquid crystal detection. Dr. Abbott's statements regarding the various surfaces described in the cited references further support Appellants' position that there would have been no reasonable expectation of success upon combining the prior teachings.

Claims 2-6, 8-11, 13, 15-20 and 22-23 depend from claim 1 and recite additional elements which define the claimed invention over the prior art. Because the Office has not articulated a reasonable expectation of success in combining the teachings of the cited documents to practice the elements of claim 1, Appellants respectfully request the Board reconsider and reverse all the obviousness rejections over either Bernard et al. or Renault et al. in view of Abbott et al.

4. Because the skilled artisan would not have had a motivation to combine the teachings of the cited documents into the method recited in the rejected claims, the rejections are improper.

In making an obviousness rejection, the Office may base its rationale on some suggestion or motivation, either in the cited references themselves or in the knowledge generally available to the artisan to combine the references. MPEP 2143(G). As further explained in section 1 above, there is simply no teaching, suggestion, or motivation in the cited documents or in the knowledge generally available to the artisan that would have led the artisan to combine the prior art teachings to arrive at the invention recited in claim 1 or recited in the claims depending from claim 1. In particular, the substitution of the detection methods described in the Abbott et al. reference for fluorescent or radioactive labeling as described by Renault et al. and Bernard et al. would not have been prompted by design incentives as the artisan could simply not expect a predictable result due to the lack of available criteria in the art for proper detection surface selection.

5. Because they appear to be based on prohibited hindsight reconstruction, the rejections are improper.

Whether a combination has a reasonable expectation of success is properly determined at the time the invention is made. *Ex Parte Erlich*, 3 USPQ2d 1011 (Bd. Pat. App. & Inter. 1986). The time of determination is essential to avoid impermissible hindsight. MPEP 2141.01(III). Because of the lack of guidance in the cited documents and in the art at the time of the invention, it appears the Office's rationale for the rejection is based on impermissible hindsight analysis using the Appellant's disclosure.

In sum, because (1) the Office has improperly ignored Declaration evidence of record presented by Appellants, resulting in a scientifically inaccurate interpretation of the cited documents; (2) the Office has not shown that there would be a reasonable expectation of success in combining the teachings of the cited documents to practice the elements of the rejected claims; and (3) the Office has not provided a credible motivation to combine the teachings of the cited documents, either within the documents themselves or within the art at the time of the invention, the obviousness rejections are clear error of law and fact. Accordingly, Appellants respectfully request the Board reconsider and reverse all the obviousness rejections over either Bernard et al. or Renault et al. in view of Abbott et al.

C. REJECTION UNDER 35 U.S.C. § 103(A) OVER BERNARD OR RENAULT IN VIEW OF ABBOTT IN FURTHER VIEW OF TANG

1. The rejection.

Claim 14 stands rejected as being unpatentably obvious over Bernard et al. or Renault et al. in view of Abbott et al, and further in view of Tang et al. (U.S. Patent 5,886,195). Tang et al. allegedly teach anti-phosphotyrosine antibodies, which may be used to measure autophosphorylation of EGFR and thereby an increase in EGF activity. The Office asserts that it would have been obvious to the artisan to employ the anti-phosphotyrosine antibodies taught by Tang et al. as the receptor molecules on the affinity substrate in a method for detecting a ligand based on Bernard et al. and Abbott et al. or, alternatively, Renault et al. and Abbott et al.

2. Because the rejected claim depends from claim 1, and Tang et al. fail to cure the deficiencies of the other combined cited documents, the rejection is improper.

The Tang et al. reference fails to cure the deficiencies in Bernard et al., Renault et al., and Abbott et al., as discussed above. Tang et al. and the additional references simply do not teach nor do they contemplate a ligand detection method having an affinity microcontact stamping step combined with a ligand detection step of contacting liquid crystal with a detection surface. In view of Apellants' arguments above, Appellants respectfully request that the Board reconsider and reverse this rejection.

D. REJECTIONS UNDER 35 U.S.C. § 103(A) OVER BERNARD OR RENAULT IN VIEW OF ABBOTT IN FURTHER VIEW OF CHOI

1. The rejection.

Claim 21 stands rejected as being unpatentably obvious over Bernard et al. or Renault et al. in view of Abbott et al, and further in view of Choi et al. (U.S. Patent 6,292,296). Choi et al. allegedly teach photo-alignment in liquid crystal devices. The Office asserts that it would have been obvious to the artisan to employ the photo-alignment with ultraviolet light as taught by Choi et al. in order to align the liquid crystal detection surface while avoiding the known disadvantages of other methods.

2. Because the rejected claim depends from claim 1, and Choi et al. fail to cure the deficiencies of the other combined cited documents, the rejection is improper.

The Choi et al. reference fails to cure the deficiencies in Bernard et al., Renault et al., and Abbott et al., as discussed above. Choi et al. and the additional references simply do not teach nor do they contemplate a ligand detection method having an affinity microcontact stamping step combined with a ligand detection step of contacting liquid crystal with a detection surface. In view of Appellant's arguments above, Appellants respectfully request that the Board reconsider and reverse this rejection.

VIII. CONCLUSION

For all of the foregoing reasons, Appellants respectfully submit that all the grounds of rejection of claims 1-6, 10, 11, and 14-23 on appeal are in error and respectfully request that the rejections be reversed.

The required appeal brief filing fee is included with this submission. In addition, to make this submission timely, a petition and fee for a Five-Month Extension of Time is also included. No additional fees are believed due, but if any additional fees are required in this application, please charge the required fees to Deposit Account No. 17-0055.

Respectfully submitted,

Dated: January 2, 2009

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APPENDIX A

CLAIMS OF PATENT APPLICATION 10/711,51 UNDER APPEAL

1. A method for detecting a ligand in a sample comprising:

(a) contacting a sample having a ligand with an affinity substrate, wherein the affinity substrate comprises a receptor capable of specifically binding said ligand, the receptor binding the ligand upon contact with the sample;

(b) contacting the affinity substrate with a detection surface, wherein the ligand which is bound to the receptor is transferred to the detection surface; and

(c) detecting the presence of the ligand on the detection surface by contacting the detection surface with a liquid crystal, wherein the presence of the ligand on the detection surface is detected by a change in the orientation of the liquid crystal contacted with the detection surface.

2. The method according to claim 1, further comprising:

(d) washing the affinity substrate after (a);

(e) washing the detection surface after (b); or

(f) both (d) and (e).

3. The method according to claim 1, wherein the receptor or ligand comprises a biomolecule, a biomolecule recognition agent, a peptide, a polypeptide, a protein, a carbohydrate, a toxin, a metal, a heavy metal, a chelator, a pathogen, a virus, a bacterium, a mammalian cell or part of a mammalian cell, a nucleic acid, a nucleic acid analog or mimic, a sugar, an antibody, a Fab, an organic molecule, a lipid, a phospholipid, a drug, a chemical agent, a pesticide or a herbicide.

4. The method according to claim 1, wherein the affinity substrate comprises a polymer, a silica material, a metal or a metal oxide.

5. The method according to claim 1, wherein the affinity substrate comprises polydimethylsiloxane (PDMS).

6. The method according to claim 5, wherein the PDMS of the affinity substrate is further terminated by an antibody which acts as the receptor capable of specifically binding said ligand, the antibody binding the protein ligand upon contact with the sample.

10. The method according to claim 1, wherein the receptor is bound to the affinity substrate via one or more linking moieties.

11. The method according to claim 1, wherein the amount of ligand present in the sample is quantified.

14. The method according to claim 1, wherein the receptor comprised by the affinity substrate is capable of detecting presence of protein phosphorylation in Epidermal Growth Factor Receptor (EGFR) residues.

15. The method according to claim 1, wherein the detection surface comprises a self-assembled monolayer.

16. The method according to claim 15, wherein the self-assembled monolayer comprises an amine, alkanethiol or organosulfur compound.

17. The method according to claim 15, wherein the self-assembled monolayer is pretreated with an acid prior to (b).

18. The method according to claim 1, wherein contacting the affinity substrate with the detection surface is performed on at least a portion of the affinity substrate that is curved.

19. The method according to claim 1, wherein the detection surface causes homeotropic anchoring in the absence of captured ligand.

20. The method according to claim 1, wherein the liquid crystal comprises a nematic liquid crystal, smectic liquid crystal, polymeric liquid crystal, lyotropic liquid crystal, chromonic liquid crystal, frustrated liquid crystals, thermotropic liquid crystal, columnar liquid crystal, nematic discotic liquid crystal, calamitic nematic liquid crystal, ferroelectric liquid crystal, discoid liquid crystal, or cholesteric liquid crystal.

21. The method according to claim 1, wherein the liquid crystal is pretreated by illumination with UV light.

22. The method according to claim 1, wherein the liquid crystal comprises 4-cyano-4'-pentylbiphenyl (5CB), or doped salt thereof.

23. The method according to claim 1, wherein orientation of the liquid crystal is detected optically or electrically.

APPENDIX B
EVIDENCE

A copy of the following item of evidence is attached:

Declaration under 37 C.F.R. §1.132 of Nicholas L. Abbott, dated October 9, 2007. This evidence was submitted and entered into the record with Appellants' Office Action response filed on October 10, 2007.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Applicant:	ABBOTT, Nicholas L.
Application No.:	10/711,517
Filing Date:	September 23, 2004
Title:	USING LIQUID CRYSTALS TO DETECT AFFINITY MICOCONTACT PRINTED BIOMOLECULES
Atty Docket No.:	960296.00526
Examiner:	FOSTER, Christine E.
Group Art Unit:	1641

DECLARATION UNDER RULE 1.132

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

1. I, Nicholas L. Abbott, the undersigned declare as follows:

2. All statements made herein are true to the best of my knowledge, or if made upon information and belief are believed to be true.

3. I received a Ph.D. in Chemical Engineering from Massachusetts Institute of Technology and performed my post-Doctoral work at Harvard University in the Department of Chemistry. I have been a professor of Chemical and Biological Engineering at the University of Wisconsin-Madison since 1998. My areas of research interest include liquid crystal technology, interfacial phenomena, colloid chemistry, nano-scale science and polymers. I have over 150 peer reviewed publications in these fields.

4. I am a co-inventor of the above captioned patent application. Accordingly, I am completely familiar with the subject matter of this patent application including the claims. I have also reviewed the latest Office Action mailed April 10, 2007 and have read the various

objections/rejections described therein. I am providing this declaration to address the obviousness rejection raised by the U.S. Patent and Trademark Office.

5. The Office is correct in noting that my issued US patent 6,852, 285 B2 does make reference to microcontact printing. Column 7 of the patent reads:

> The substrate can also be patterned using techniques such as photolithography (Kleinfield et al., *J. Neurosci.* 8:4098–120 (1998)), photoetching, chemical etching and microcontact printing (Kumar et al., *Langmuir* 10: 1498–511 (1994)). Other techniques for forming patterns on a substrate will be readily apparent to those of skill in the art.
>
> The size and complexity of the pattern on the substrate is limited only by the resolution of the technique utilized and the purpose for which the pattern is intended. For example, using microcontact printing, features as small as 200 nm have been layered onto a substrate. See, Xia, Y.; Whitesides, G., *J. Am. Chem. Soc.* 117:3274–75 (1995). Similarly, using photolithography, patterns with features as small as 1 μm have been produced. See, Hickman et al., *J. Vac. Sci. Technol.* 12:607–16(1994). Patterns which are useful in the present invention include those which comprise features such as wells, enclosures, partitions, recesses, inlets, outlets, channels, troughs, diffraction gratings and the like.

6. The above text (column 17) is part of a description of materials and methods that can be used to fabricate surfaces (referred to as "substrates" in the patent) on which molecular interactions can be detected using liquid crystals. In support of this comment, I note that column 17 is part of a section of text that starts in column 14, and is labeled "A. Substrates". This section of text describes various materials that can be used to fabricate surfaces, including inorganic crystals, and glasses and inorganic oxides, metals, and organic polymers. In this context, text in column 17 notes that various means can be used to process these materials, including photolithography, photoetching, chemical etching and microcontact printing. In preparing this text, we made reference to Kumar et al (Langmuir, 10, 1498-1511, 1994) and Xia and Whitesides (JACS, 117, 3274-75, 1995). These two papers accurately describe the use of microcontact printing (but not affinity microcontact printing) as a tool for microfabrication of structured surfaces, including gold and silicon micro and nanostructures. In particular, these papers point out that microcontact printing permits fabrication of structures as small as 200nm, which is reiterated in column 17 of the application. Whereas the column 17 text and the above references clearly describe microcontact printing as a tool for fabrication of surfaces, neither the

column 17 text nor the above references suggest that microcontact printing can be used to deliver analytes to a surface for detection of molecular interactions using liquid crystal. It is this use of "affinity" microcontact printing (i.e., a means of delivery of an analyte to a surface) that is described and claimed in my present patent application. As well, my present patent application does not mention the use of affinity microcontact printing as a tool for microfabrication of device surfaces.

7. This declaration is made with knowledge that willful false statements and the like are punishable by fine or imprisonment, or both under 18 USC Sec. 1001, and may jeopardize the validity of the subject patent application or any patent issuing thereon.

Dated: OCTOBER 9, 2007

NLAbbott
Nicholas L. Abbott

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APPENDIX C

RELATED PROCEEDINGS

There are no decisions in related proceedings.